



[BILLING CODE 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Request for Information on the Proposed Framework for Developing Study Content and Protocols for the National Children's Study

SUMMARY: The National Children's Study (NCS) is soliciting comments and suggestions from the public on the proposed Study content framework. The questions solicited in this Request for Information (RFI) focus on the validity and acceptability of the using a composite outcome for the higher-level functions of a healthy 21-year-old person as an important operational construct to help frame data collection throughout the duration of the study. Responses to this RFI will be used to inform Study protocol development.

DATES: The National Children's Study Request for Information is open for public comment for a period of 30 days. Comments must be received by [INSERT THE DATE 30 DAYS FOLLOWING THE DATE OF PUBLICATION IN THE FEDERAL REGISTER] to ensure consideration. After the public comment period has closed, the comments received by the NCS will be considered in a timely manner by the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Children's Study.

ADDRESSES: Questions about this request for information should be directed to Kate Winseck, MSW, The National Children's Study, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, 6100 Executive Blvd., Rm. 5C01, Bethesda, MD 20891, NCS_RFI@mail.nih.gov, 301-594-9147.

SUPPLEMENTARY INFORMATION: The National Children's Study is a congressionally-mandated longitudinal birth cohort study intended to examine the effects of environmental exposures on the growth, development, and wellbeing of children. The NCS was mandated by the Children's Health Act of 2000 (Public Law 106-310).

1. Goals and Requirements

The primary objective of the NCS is to conduct a national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on children's health and development. These factors include environmental exposures (with a broad definition of environment) and biological/genetic contexts. The Study objectives stated in the Children's Health Act of 2000 include: (1) evaluate the effects of both chronic and intermittent exposures on child health and human development; (2) investigate basic mechanisms of developmental disorders and environmental factors; (3) incorporate behavioral, emotional, educational, and contextual consequences to enable a complete assessment of the physical, chemical, biological and psychosocial environmental influences on children's well-being; (4) gather data from diverse populations of children including prenatal exposures; and (5) consider health disparities among children.

2. Proposed Study Content Framework

The NCS proposes to organize data collection priorities to support measurement of health and healthy development at critical stages. This requires understanding and identifying known and potential factors that may influence health outcomes and characteristics along the developmental spectrum. For example, data collected during pregnancy are designed to look not only at antecedents of disease but also to look for factors associated with health. Which exposures are associated with a healthy, full term infant? What factors are predictive of a normal birth weight? What factors are associated with normal neurologic development? Areas that will be examined include, but are not limited to (1) physical factors such as maternal and paternal height, weight and Body Mass Index (BMI); (2) health behaviors such as sleep, diet and physical activity; (3) outcomes of past pregnancies and other medical conditions and history; (4) medication use (including alternative and complementary medicines); (5) presence or absence of components of the physical environment, such as noise, mold and mildew, pets, chemicals, and environmental tobacco smoke; and (6) psychosocial factors, such as social support, social networks, and psychological well-being and other factors that may protect and mediate reactions to stress. Biological and environmental samples will be collected to allow examination of in-utero exposures.

The NCS intends to follow all children from birth until they reach age 21, an endpoint consistent with the Food and Drug Administration Amendments Act of 2007 that defines “pediatric patients” as “those who are 21 years of age or younger at the time of diagnosis or treatment (FDA Amendments Act of 2007).” As such it is important to identify the characteristics of a healthy 21-year-old person. Reaching age 21 is one of

many important developmental milestones and it serves as a useful life stage for illustration of how the NCS data collection framework can be organized.

To ensure the Study content framework is comprehensive, the NCS is working with subject matter experts to characterize health. As developmental trajectories are multi-dimensional, multi-directional, and multi-level, this effort not only helps characterize the distal end of the childhood developmental trajectory, but also identifies potential antecedent factors that could be measured earlier in life in assessing exposures that may contribute to later outcomes. For example, supportive family relationships during adolescence has been associated with positive outcomes ranging from reduced risk of poor mental health to higher levels of interpersonal and occupational functioning; these outcomes being independent of any effect of gender, socioeconomic status, or family disruption, for example death or divorce (Child Adolescent Mental Health 16(1): 30-37).

At 21 years old, the thriving individual is a manifestation of complex, dynamic, non-linear developmental processes that are products of personal characteristics (including genetics), person-to-person, and person-to-environment interactions in the broadest sense. This characterization is consistent with the World Health Organization (WHO) construct (<http://www.who.int/hia/evidence/doh/en/>) which recognizes the following determinants of health:

- The social and economic environment
- The physical environment
- The person's individual characteristics and behaviors

A healthy 21-year-old person may possess such attributes as a BMI between 19 and 25, blood pressure about 120/80 mm mercury, sound mental health, and the ability to develop and maintain relationships with other people. A healthy 21-year-old person may be able to obtain employment if desired or circumstances warrant. A healthy 21-year-old person should be able to provide food, clothing, and shelter for themselves and, if desired or if circumstances warrant, for others. One would expect that a 21-year-old person would possess a solid foundation in literacy (including written and oral communication skills), numeracy, and problem solving skills. As young adults, they may have positive relationships with friends or family, a network of peers, and feel that they are part of a community. Furthermore, a healthy 21-year-old person is not defined on the basis of an individual who is free of disease or disability. If an individual has a limitation, she or he may still be able to function well, and even thrive, in society with the proper access to care, social support, and adaptations.

The NCS will measure health as well as the presence or absence of disease-related signs, symptoms, and limitations. This requires a data collection protocol that captures a full description of an individual—a health profile—rather than just known determinants of disease and subsequent outcomes. This is consistent with the Life Course Health Development model which “not only measures an individual’s deficits but also calculates his or her health assets (The Millbank Quarterly 80(3): 433).”

As an organizing principle, the construction of a data collection approach around the characteristics of a healthy 21-year-old person allows the NCS to identify and measure the full range of experiences that may later influence individual outcomes. Measures must address the range of potential influences, from individuals, family, peers, the

environment, communities or the larger society. This collection will supplement the conventional measurement of known or theorized antecedents of disease-related outcomes. The NCS does not intend to evaluate each participant using a particular paradigm as a preferred outcome, but rather to ensure that generally accepted health characteristics can be captured across the spectrum of the NCS. The NCS is not and cannot be a national screening program for various conditions but should be able to identify a wide range of phenotypic characteristics. The NCS will emphasize recording primary signs and symptoms, capacities and limitations, and a description of the whole person rather than diagnosing individuals as having particular diseases or conditions. Nonetheless, all relevant information from medical records, therapeutic interventions, and descriptions from participants and care takers will be captured and become part of the analytic data sets.

In such a model, however, the linking of a particular participant with a particular disease or condition may not offer all the necessary or even accurate information about either that individual or the population at large. By maintaining a focus on primary signs and symptoms, performance, any limitations, trends, developmental progress, experience, adaptation to changes in environment and context and relationships to the people and world around each participant, the NCS intends to maintain flexibility and precision for future analyses.

Health disparities will be addressed using a definition from the Centers for Disease Control and Prevention that notes disease burden, injury, violence, and health potential as key parameters (CDC, HHS, 2008). Each participant in the NCS will be evaluated for each of these parameters, regardless of any other demographic or

socioeconomic characteristics. Through this approach, the NCS can maintain continuity of purpose through the ever-present changes in a dynamic society.

In sum, the NCS is proposing the use of a framework of distal outcomes, health determinants, primary signs and symptoms, phenotypic and environmental descriptions, and capture of parameters associated with health disparities to guide the selection of the specific assessments along with their sequence and frequency. Related materials with additional information can be found here:

<http://www.nationalchildrensstudy.gov/about/organization/advisorycommittee/Pages/January-2014-NCSAC-Meeting-Briefing-Book.aspx>

3. Information Requested

This RFI invites the scientific community, health professionals, and the general public to provide comments and suggestions on the proposed framework of using the characteristics of a healthy, functional 21-year-old person, plus the other principles and factors noted, above for developing Study content and protocols. Given the requirements as stated in the Children's Health Act of 2000, please include in responses to the questions below whether the Study proposed content framework balances the complex requirements.

1. Please comment on the validity and acceptability of using a composite outcome—the higher-level functions of a healthy 21-year-old person—as an operational construct to help frame data collection.
2. Are there additional outcomes or developmental endpoints that should be considered?

3. What factors should the NCS use to prioritize assessments? Some examples of factors to consider are:

- a. Potential public health impact
- b. Technical feasibility, including timing of data collection with regard to potential developmental vulnerability
- c. Scientific opportunity to address knowledge gaps and illuminate developmental pathways

This RFI is for planning purposes only and should not be construed as a solicitation for applications or proposals, or as an obligation in any way on the part of the United States Federal government. The Federal government will not pay for the preparation of any information submitted or for the government's use. Additionally, the government cannot guarantee the confidentiality of the information provided.

Dated: __January 15, 2014.

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National Children's Study

Eunice Kennedy Shriver National Institute of Child Health and Human Development

[FR Doc. 2014-01339 Filed 01/22/2014 at 8:45 am; Publication Date: 01/23/2014]